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Structural characterization of peptides from phage-display libraries

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Phage display procedures are a useful technology for mapping epitopes and a number of other applications. Phage-displayed peptide libraries are rich in information due to their ability to sample a large number of mutations in a single experiment. This advantage is frequently underexploited by overemphasizing the value of the higher affinity sequences or the consensus motif, disregarding the large amount of information encoded in the sequence variability observed. This information can be utilized to create structural 3D models of the bound peptide, provided enough homology relates the members of the peptide library. A technique to achieve this goal is presented. The technique affords a fully automated protocol, based on Feedback Restrain Molecular Dynamics (FRMD). The protocol searches a consensus 3D motif that satisfies the geometric requirements of all sequences considered simultaneously. The search is performed using a molecular dynamics procedure for each separate peptide sequence considered, with the structural information from each trajectory being shared with each other by means of a series of auto-evaluated restraints, whose value is automatically adjusted following the rules of the FRMD procedure. The procedure is fast, easily parallelizable and fully independent of the starting point. Here we present the results of the application of this technique to several targets including EPO and streptavidin peptide analogs obtained from phage display libraries. This work has been funded in part with funds from the NCI-NIH (Contract No. NO1-CO-12400). The contents of this publication do not necessarily reflect the views or policies of the DHHS, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.